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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/339,818	06/25/1999	MARK E. DAVIS	038134-50010	3090
28120	7590	01/25/2005	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			CRANE, LAWRENCE E	
			ART UNIT	PAPER NUMBER
			1623	
DATE MAILED: 01/25/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/339,818	<b>Applicant(s)</b> DAVIS ET AL.	
	<b>Examiner</b> L. E. Crane	<b>Art Unit</b> 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on September 20, 2004 (Response).
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3,6-10,18,24-26,30-34,44,46 and 58-64 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,6-10,18,24-26,30-34,44,46 and 58-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

No claims have been cancelled, no claims have been amended, no further amendments to the disclosure have been submitted, and no additional new claims have been added as per the response filed September 20, 2004. No additional Information Disclosure Statements (IDSs) have been submitted as of the mailing date of this Office action.

Claims 1-3, 6-10, 18, 24-26, 30-34, 44, 46 and 58-64 remain in the case.

Claims 1-2, 7-10, 18, 24-26, 31-34, 44, 46 and 58-64 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 1-2, 7-10, 18, 24-26, 31-34, 44, 46 and 58-64 functional terminology is present which describes chemical functionalities of a “cyclodextrin”-containing species, a “comonomer A,” and the like, but fails to further define same in sufficient detail to permit one of ordinary skill to be able to determine the particular chemical species being referred to; a metes and bounds problem. For example, in claim 1 the terms “water soluble” and “linear” modify the term “cyclodextrin copolymer,” but fail to define what particular chemical functional groups and chemical linkages are present between the cyclodextrin and comonomer A. The chemical structure or structures of “comonomer A” is/are not defined in any way in claim 1. In claim 24 precursors to the polymer are defined as being disubstituted (“cyclodextrin comonomer precursor”) and “comonomer A” is described as being “capable of displacing said leaving groups to form a linear cyclodextrin copolymer having repeating groups ... .” Claim 25 defines the cyclodextrin reactant, but is incomplete for failure to define structural identity of the chemical crosslinkers (comonomer A) which are needed to produce the product. Claim 31 adds a “ligand” attachment step, but fails to define a chemical reagent for effecting such a step. Claim 32 narrows the subject matter slightly, but fails to define what “aminating reagent” or “reagents” are converting the di-iodocyclodextrins of claim 25 to “diamino” analogues. Claim 58 is directed to reacting a “cyclodextrin derivative modified to bear one reactive site at each of exactly two positions,” suggesting that either valence rules are being violated, or that applicant has not clearly described the subject matter. Similarly, claim 58 is directed to a “linker” which has “exactly two reactive moieties capable of forming a covalent bound with the reactive the reactive sites [of the cyclodextrin derivative] under polymerization conditions,” but has failed to define the chemical identity or identities of the

“reactive moieties” or the particular “polymerization conditions” being referred to. See also claim 61. See also compound claims 59, 60 and 62-64 which have the same or similar problems following from reliance on functional terminology.

Applicant's arguments filed September 20, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant has not elected to respond to the instant grounds of rejection. Therefore, said rejection has been maintained.

Applicant's arguments filed November 10, 2003 have been fully considered but they are not deemed to be persuasive. (verbatim repeat from the previous Office action)

As applicant notes in the response of November 10, 2003, the question is whether the claims “set out and circumscribe a particular subject matter with a reasonable degree of particularity.” (emphasis added). In light of the instant newly cited prior art (art rejection below) kindly supplied previously by applicant, it is evident that applicant's disclosure fails to describe the work of the ‘194 reference, but that the generic claims listed in the rejection below read on said reference. Therefore, examiner suggests that applicant should now seek to avoid said reference by limiting the instant claims to a much less generic, and much more structurally specific, scope. In so doing, examiner suggests the possibility that the instant grounds of rejection could also be avoided.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

“A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.”

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.”

Claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 are rejected under 35 U.S.C. §102 (b) as being anticipated by **Toppan Printing Co. ‘194** (PTO-1449 ref. **BM**).

Applicant is referred to the noted reference wherein a large number of exemplifications disclose linear polymers of  $\alpha$ -,  $\beta$ - and  $\gamma$ -cyclodextrins wherein cyclodextrin intermediates (some of which are very similar or identical to those disclosed herein) are converted into various enzyme-degradable polymers with urethane, urea, unsaturated ester, ester, carbonate, amide and sulfone linkages between the cyclodextrin units. The cyclodextrin polymer products are required to be linear by the protecting group strategy applied or by using bridged cyclodextrin precursors. See examples illustrated by oligomeric structures at pages 18-19, 27-29, 31-32 and 37-39. Note also that the proposed structures (only primary hydroxyl shown to react) do not exclude the possibility that the actual products produced result from reaction with primary **and/or** secondary cyclodextrin hydroxyls; e.g. boronic acids and aldehydes are both notoriously well known to form stable cyclic compounds with vicinal dihydroxy compounds (glycols), a functionality found only on the secondary (open) side of cyclodextrins. In addition, at page 26, lines 14-15, reference is made to "low-molecular weight oligomers" ... "extracted with hot ethanol," a class of oligomeric compounds which are presumed to have some water solubility. And lastly, at page 8 of the '194 reference, applicant is referred to the conversion of compound "[6]" into compound "[B]" at lines 35-45 of column 2 and associated explanatory text as anticipating the cited method of making claims. Therefore, the cited reference is deemed anticipate both of the generic structures of instant claim 1 and methods of making same.

Applicant's arguments filed September 20, 2004 have been fully considered but they are not deemed to be persuasive.

Applicant has argued that the main product is not water soluble. Examiner agrees, but notes the lower molecular weight biproduct is the subject matter specifically referred to and that its water solubility is still deemed to be probable, but examiner acknowledges that said solubility has not been not specifically commented on or otherwise specifically established within the noted reference.

Claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 are rejected under 35 U.S.C. §102(b) as being anticipated by Ceccato et al. (PTO-892 ref. VA).

Applicant is referred to p. 5096, column 1, last two sentences in the second full paragraph, wherein the generation of "Molecular Tube" (MT; see Figure 2 at p. 5095) from its

precursor is disclosed. The subsequent separation of PEG-MT and MT by elution with water (some water solubility of MT is required) through a Sephadex column is also disclosed and illustrated in Figure 4. This disclosure also notes at page 5098, column 2, beginning 5 lines from the end of the column, that the MT synthesized herein is longer (and higher molecular weight) than that synthesized by Harada et al. (cited in the following rejection). And this reference teaches at p. 5099, first sentence of the conclusion, that “ $\alpha$ -,  $\beta$ - and  $\gamma$ -cyclodextrins” are all capable of forming similar “crystalline complexes when treated with a proper long-chain polymer,” implying that the formation of a “Molecular Tube” is within the purview of the ordinary practitioner for all three cyclodextrins once a “Molecular Necklace” has been formed by contacting the selected cyclodextrin with “a proper long-chain polymer.”

Applicant's arguments with respect to claims **1-3, 7, 24-26, 32-33, 58-60 and 62-64** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **1-3, 7, 24-26, 32-33, 58-60 and 62-64** are rejected under 35 U.S.C. §102(b) as being anticipated by **Harada et al.** (PTO-892 ref. **XA**).

Applicant is referred to Figure 1 (p. 516, “Molecular Tube”) and columns 1-2 at page 518 wherein water solubility is specifically disclosed at least twice.

Applicant's arguments with respect to claims **1-3, 7, 24-26, 32-33, 58-60 and 62-64** have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims **1-3, 7, 24-26, 32-33, 58-60 and 62-64** are rejected under 35 U.S.C. §102(b) as being anticipated by **Uekama et al. (I)** (PTO-892 ref. **ZA**).

Applicant is requested to note the abstract at page 27 wherein water soluble polymers of all three common cyclodextrins and epichlorohydrin are disclosed. In addition, Table 1 at page 28 indicates average molecular weights for the copolymers which by their sizes require that a substantial proportion of the contents of what are mixtures must be linear copolymers; e.g.  $\gamma$ -CD-C3- $\gamma$ -CD has a molecular weight slightly above 2600 which is just slightly below the overall average of 3000 listed for the mixture generated from contacting this cyclodextrin with epichlorohydrin.

Applicant's arguments with respect to claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 are rejected under 35 U.S.C. §102(b) as being anticipated by **Uekama et al. (II)** (PTO-892 ref. UB).

Applicant is referred to the Title, the Abstract, and the Results and Discussion section beginning at page 37 wherein the disclosed subject matter which anticipates the instant claimed subject matter is summarized and then described in detail.

Applicant's arguments with respect to claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 have been considered but are deemed to be moot in view of the new grounds of rejection.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made."

Claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 are rejected under 35 U.S.C. §103(a) as being unpatentable over **Harada et al.** (PTO-892 ref. XA) in view of **Ceccato et al.** (PTO-892 ref. VA).

The instant claims are directed to "water soluble, linear cyclodextrin copolymer comprising repeating units of ... a substituted or unsubstituted cyclodextrin monomer and ... a comonomer" wherein there is no structural information whatsoever in claim 1 defining the chemical structure of the comonomer, or the cyclodextrin substituents or the location(s) of said substituents. Quotations are taken directly from claim 1.

**Harada et al.** discloses compounds referred to generically as "Molecular Necklace" and Molecular Tube (MT)," the latter of which reads directly on the instant claims and also specifies water solubility, including NMR-spectroscopic examination in solutions of MT and D<sub>2</sub>O.

**Harada et al.** does not expressly disclose that  $\beta$ - and  $\gamma$ -cyclodextrins are capable of being incorporated into a "Molecular Tube," or how to make such a product.

**Ceccato et al.** discloses that " $\alpha$ -,  $\beta$ - and  $\gamma$ -cyclodextrins" are all capable of forming similar "crystalline complexes when treated with a proper long-chain polymer," implying that the formation of a "Molecular Tube" is within the purview of the ordinary practitioner for all three cyclodextrins once a "Molecular Necklace" has been formed by contacting the selected cyclodextrin with "a proper long-chain polymer."

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Ceccato et al. to the method of Harada et al. in order to make "Molecular Tube" compounds which are of sufficiently low molecular weight from all three common cyclodextrins so as to be unquestionably water soluble in each case.

One having ordinary skill in the art would have been motivated to combine these references because both references deal with the synthesis and structural analysis of cyclodextrin-containing "Molecular Tubes," and because the Ceccato et al. reference makes specific reference to three of the earlier disclosures of Harada et al. in a detailed discussion of this specific subject matter area.

Therefore, the instant compound claims incorporation of "Molecular Tubes" would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments with respect to claims 1-3, 7, 24-26, 32-33, 58-60 and 62-64 have been considered but are deemed to be moot in view of the new grounds of rejection.

Claims 6, 8-10, 18, 30-31, 34, 44, 46 and 61 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. §112.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

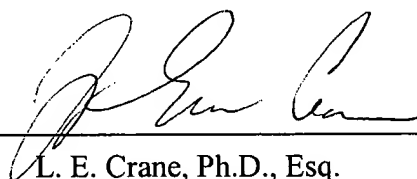


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

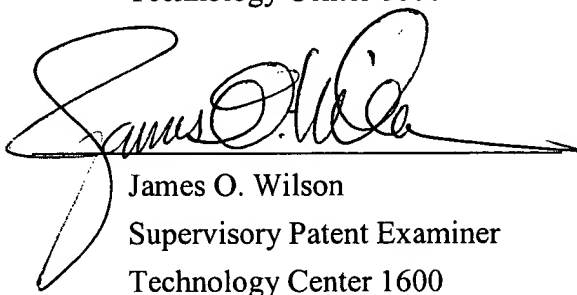
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